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THE ROLE OF CREATINE PHOSPHATE IN THE HUMAN BODY

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Abstract*. Creatine phosphate is a reserve of explosive energy. Creatine is a substance of skeletal muscles, myocardium, and nervous tissue. In the form of creatine phosphate, creatine is a "depot" of macroergic bonds and is used for rapid resynthesis of ATP during cell work. Creatine phosphate was first isolated from muscle tissue in 1927 [1]. However, the study of its role and influence on various processes in the human body continues to this day. This is explained by the fact that creatine phosphate is an energy substrate for the rapid synthesis of ATP under anaerobic conditions. That is, the formation of ATP does not require oxygen and the participation of mitochondria. In turn, ATP is a universal source of energy in the human body.*

Keywords*: creatine, ATP, Creatine phosphate, creatine phosphokinase, resynthesis, rephosphorylated, phosphofructokinase, ischemia, anoxia, myocardium, skin, hair.*

Introduction.

The role of creatine in muscle tissue is especially significant. Creatine phosphate ensures urgent resynthesis of ATP in the first seconds of work (5-10 sec), when no other energy sources (anaerobic glycolysis, aerobic oxidation of glucose, β-oxidation of fatty acids) are yet activated and the blood supply to the muscle is not increased. In nervous tissue cells, creatine phosphate maintains cell viability in the absence of oxygen.

This energy is necessary for the synthesis of substances, muscle contraction, and ion transport [2, 3]. ATP is low, about 4.5-5 mmol/kg muscle tissue. Therefore, its constant resynthesis occurs in the body [2]. Aerobic resynthesis is carried out through oxidative phosphorylation, anaerobic resynthesis is carried out by the glycolytic process, creatine phosphokinase reaction. The creatine phosphokinase reaction is based on the synthesis of ATP due to the hydrolysis of the phosphamide bond (N-P) of creatine phosphate (CrP) [2].

Schematically, this reaction can be written as follows:

MgADP + CrP2- + H+ MgATP2- + Cr (creatine)

This is a reversible enzymatic reaction. Catalysis is carried out by creatine kinase (creatine phosphokinase, CPK, CK) [4]. As early as 1962, it was shown that when creatine kinase was inhibited in experimental models, ATP levels rapidly decreased, resulting in a block in muscle contraction. [5].

MATERIALS AND METHODS

Inside cells, creatine phosphate functions as a shuttle between the site of ATP production and use. In mitochondria, ATP is formed through oxidative phosphorylation, which cannot be transported across the outer mitochondrial membrane [12]. Therefore, in the intermembrane space of mitochondria, ATP phosphorylates creatine to form creatine phosphate. It is transported across

the mitochondrial membrane into the sarcoplasm of cells. In the sarcoplasm, if necessary (for example, during contraction of myofibrils), creatine phosphate interacts with ADP and ATP and creatine are formed. Creatine is returned to the mitochondria where it is rephosphorylated. [13]. This process is called the “creatine phosphate shuttle”. The enzyme “creatine phosphate shuttle” is creatine kinase. Mitochondrial isoforms of creatine kinase catalyze the formation of creatine phosphate in mitochondria. And myofibrillar isoforms of this enzyme cleave the phosphate group from creatine phosphate and transfer it to ADP to form creatine and ATP.

The main function of creatine phosphate is energy. Already at 0.5-0.7 s of intense physical work, the creatine phosphokinase process reaches its maximum power - 3.8 kJ/kg/min [3, 16] and for 15-30 s plays a decisive role in the energy supply of short-term work of maximum intensity [3]. For example, 100 m running, jumping, throwing, weightlifting exercises. Creatine phosphate is quickly resynthesized when work power decreases or during the rest period after exercise, when aerobic resynthesis of ATP predominates. It can fully recover in 60–120 s [16, 17]. Reuse of the creatine phosphokinase process may be limited by high lactate concentrations and low pH values as an inhibitor of SA [3, 16, 18, 19]. For example, it is easier to accelerate at the finish line by using the power of the creatine phosphokinase process when running long distances than short ones.

Skeletal muscle contains about 90% of the human body's creatine phosphate. In this case, the ratio of creatine phosphate to free creatine is ~67% to ~33%, respectively [6, 7]. About 2% of the body's creatine is lost daily as a result of the non-enzymatic breakdown of creatine to creatinine [8, 9].

The creatine phosphokinase reaction provides rapid ATP synthesis in situations of high metabolic demand. For example, during physical activity of high power and intensity [3].

It has been shown that creatine kinase is specifically associated with glycolytic enzymes that either participate in the formation of ATP, for example, pyruvate kinase (PK) [20], or regulate glycolysis, for example, phosphofructokinase [21]. Thus, ATP, which is produced in glycolysis, can reduce creatine to creatine phosphate. This prevents creatine phosphate depletion under anaerobic conditions and inhibits phosphofructokinase (PFK), which reduces activity at high ATP concentrations. It has been shown that the muscles of patients with PFK deficiency demonstrate a sharp slowdown in creatinine phosphorus recovery after exercise.

The purpose of this review article is to detail the mechanism of the creatine phosphokinase reaction, describe the role of creatine phosphate in metabolism and energy, and demonstrate its use in exercise, recovery, and other clinical conditions, based on recent research.

RESULT AND DISCUSSIONS

Creatine phosphate is an energy substrate of the myocardium. A large number of studies of heart failure show CrP depletion during ischemia, anoxia, and toxic cardiomyopathies [1, 13, 24], while the creatine phosphate/ATP ratio in the myocardium decreases [23]. The myocardial creatine phosphate/ATP ratio was also shown to be a significant independent predictor of cardiovascular mortality (5% for CrP/ATP ratio >1.6; 10% for CrP/ATP ratio <1.6) in a multivariate analysis of patients with heart failure.

CrP interacts with membrane phospholipids. Its opposite charges interact with charged phospholipids located on either side of the sarcolemma [1]. This results in membrane protection and stabilization, influencing additional membrane processes such as ion homeostasis and cellular signaling. Stabilization of cell membranes, in turn, prevents cell lysis [25, 26]. Creatine phosphate

and creatine kinase stabilize the permeability of mitochondrial membranes [14]. Moreover, the antioxidant mechanism of action of creatine phosphate has been demonstrated, confirming that it acts on the lipid bilayer, organizing membrane phospholipids in the membrane structure [27] The membrane-stabilizing effect of creatine phosphate underlies its ability to protect the heart from ischemic damage and oxidative stress. Free oxygen radicals are considered the main causes of myocardial damage, especially during ischemia and reperfusion [1, 23]. Creatine phosphate stabilizes the adenylate kinase (myokinase) reaction. In sports biochemistry, it is considered as an emergency mechanism that ensures ATP resynthesis in conditions when other ATP resynthesis pathways are ineffective [3]. The adenylate kinase reaction consists of the formation of ATP and AMP at the expense of two ADPs.

ADP + ADP ↔ ATP + AMP

In this case, AMP is easily deaminated to form inosinic acid [2, 3]. Creatine phosphate has been shown to inhibit the enzymes of AMP catabolism: AMP deaminase and 50-nucleotidase [26]. When 50-nucleotidase activity is inhibited, the adenine structure is retained as AMP, and since the adenylate kinase reaction to form ADP is reversible, ADP and ATP are still formed. Creatine phosphate also preserves the adenine nucleotide pool by affecting de novo synthesis. Creatine phosphate reverses the inhibition of ADP phosphoribosyl pyrophosphate synthase (PRPP), an enzyme that catalyzes the formation of phosphoribosyl pyrophosphate from ribose 5-phosphate and ATP, leading to the resynthesis of adenine nucleotides [26].

It has been shown that creatine phosphate and creatine kinase are the basis for the distribution of energy in photoreceptors (vision), are important for maintaining hearing [14], for the normal functioning of the skin [28], proliferation and hair growth [29]. Creatine phosphate promotes thermogenesis by stimulating mitochondrial ATP turnover in brown adipose tissue and is associated with M2 polarization in macrophages. Creatine phosphate metabolism in white adipocytes is impaired during obesity in both humans and mice. This leads to changes in ATP/ADP levels, which in turn weakens the activity of 5'AMP-activated protein kinase (AMPK). This enzyme (AMPK) activates the transcription of various proinflammatory genes, including the chemokine CCL2.

Conclusion.

Thus, the role of creatine phosphate in metabolism and energy is important and multifaceted. It is the first to be included in energy production during physical activity, supports myocardial function, protects and stabilizes cell membranes. Literature data indicate the ability of creatine phosphate to prevent the destructive effects of physical activity and stress on muscle fibers, to correct a number of negative consequences of intense training in athletes, and can be considered as an aid at various levels as a drug that does not have doping properties in the training process and rehabilitation.

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